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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/804,302	03/18/2004	Wilhelmus Everardus Hennink	313632001120	7804

25225 7590 06/04/2007

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EXAMINER	
SILVERMAN, ERIC E	
ART UNIT	PAPER NUMBER
1615	

MAIL DATE	DELIVERY MODE
06/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/804,302	HENNINK ET AL.	
	Examiner	Art Unit	
	Eric E. Silverman, PhD	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-12* is/are rejected.

7)☒ Claim(s) *5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11-7-05, 1-18-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election of species, filed 3/26/2007, has been received. Group II, claims 5 – 12 were elected. Although Applicants' stated that the election is with traverse, no argument was provided as to why Applicants' believe the restriction requirement was improper. As such, the election is being treated as having been made **without traverse**. Applicants' suggested that if the elected claims are found allowable, the non-elected group should be rejoined. This suggestion is moot, since the elected claims are not allowable at this time.

Claims 1 – 12 are pending. Claims 1 – 4 are withdrawn as non-elected.

Priority

Applicants' claim priority claim to 10/048,732 is acknowledged. However, it is noted that the '732 Application does not provide description and enabling support for instant claims in their entirety. Claim 5 is drawn to drug delivery systems containing homo or interpolymers of a N-(2-hydroxypropyl)methacrylamide lactate. The '732 Application only recognizes copolymers (interpolymers) of N-(2-hydroxypropyl) methacrylamide lactate to be useful in drug delivery systems. Every drug delivery system in '732 is based on micelles, which are only formed from block copolymers of N-(2-hydroxypropyl)methacrylamide lactate and a hydrophilic polymer (such as PEG). With respect to instant claims 8 and 9, the '732 Application does not teach how to make tri-block copolymers. The block copolymers in '732 are made from a PEG macroinitiator, which is used to initiate polymerization of N-(2-hydroxypropyl)methacrylamide lactate monomers. The PEG initiator species in the '732

Application is monofunctional, that is, each PEG chain has only one propagating radical after the initiation event. Such initiators are not suitable for making ABA copolymers, wherein A is hydrophilic (PEG) and B is hydrophobic (N-(2-hydroxypropyl)methacrylamide lactate). In fact, the '732 Application does not appear to envision such polymer architectures.

Even more importantly, '732 does not contemplate *controlled release* systems, nor are such disclosed or taught in that Application.

Therefore, the **effective filing date of the Application is 3/18/2004**, and the references applied against the instant claims are competent prior art under 35 USC 102(a) or (b), and 103(a).

Claim Objections

Claim 5 is objected to because it is dependent on withdrawn claim 1. Claim 6 is rejected on because it depends on withdrawn claim 4 Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 11, and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for systems comprising micelle or hydrogel forming copolymers, does not reasonably provide enablement for homopolymers or

copolymers that do not form micelles or hydrogels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claims recite a controlled release drug delivery system containing a homo or interpolymer of N-(2-hydroxypropyl)methacrylamide lactate. It should be noted that the Applicant defines "interpolymer" in the application to mean a polymer with more than one monomer. The typical term used for a polymer with more than one monomer is "copolymer". Thus, in the discussion below, these terms may be used interchangeably.

State of the prior art: The prior art recognizes that drug delivery systems comprising N-(2-hydroxypropyl)methacrylamide lactate are made from copolymers of this material. Cadee et al. (of record, see PTO 1449 filed 10/7/2005) discloses copolymers with heparin that form hydrogels, the hydrogels being useful for controlled release. Neradovic et al (see PTO 1449, filed 10/7/2005), Soga et al and Neradovic et al in Macromolecules, 2003 (see attached PTO 892) disclose the use of copolymers of

N-(2-hydroxypropyl)methacrylamide lactate and a hydrophilic polymer, typically PEG, to form micelles. These micelles are useful in controlled drug delivery.

Pointedly, the art does not recognize the use of homopolymers of N-(2-hydroxypropyl)methacrylamide lactate or of copolymers comprising N-(2-hydroxypropyl)methacrylamide lactate which cannot form micelles and which are not hydrogels, in drug delivery.

Existence of working examples/specification: The specification discloses drug delivery from micelles of N-(2-hydroxypropyl)methacrylamide lactate copolymers. Applicant also does not take into account in the specification or through working examples that N-(2-hydroxypropyl)methacrylamide lactate is not believed to form micelles or hydrogels unless it is present as part of a copolymer. This is true because N-(2-hydroxypropyl)methacrylamide lactate is quite hydrophobic, so homopolymers thereof would not self assemble in water.

Amount of experimentation necessary: In order to use the claimed invention, the artisan would have to discover how to formulate controlled release systems with N-(2-hydroxypropyl)methacrylamide lactate homo or inter polymers which are neither micelles or hydrogels (for example, blends of drug with the homopolymer of N-(2-hydroxypropyl)methacrylamide lactate). However, there is no guidance in the specification or the art on how to do this. As such, the artisan would have to essentially start from scratch; the experimentation required would therefore be undue and the claims are not fully enabled by the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5 – 12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 contains the limitation of a "polymer having a lower critical solution temperature" (by virtue of depending on withdrawn claim 1). A LCST is a property of a polymer solution, not of the polymer itself. Besides the nature of the polymer, the LCST will depend on the nature of the solvent and the other components of the solution.

The remaining claims are rejected at least for depending on claim 5 without resolving this issue.

Claim 6 recites the limitation "controlled release system" in claim 4. There is insufficient antecedent basis for this limitation in the claim.

The phrase "the hydrogel" in claim 9 lacks proper antecedent basis. Although claim 8 mentions a hydrogel, claim 9 does not depend on claim 8.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 5, 8, 9 and 12 are rejected under 35 U.S.C. 102(b) as being anticipated by Cadee et al, of record.

Cadee teaches N-(2-hydroxypropyl)methacrylamide dilactate coupled to dextran and formed into a hydrogel (6879, section 2.6). Dextran is a homing device according to the definition in the specification, since dextran is a polysaccharide and is thus a "homing device" for polysaccharases.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 5 – 7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic et al., Macromolecules, **2001**, *34*, 7589 – 7591, of record.

Neradovic discloses a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate copolymer and micelles made from AB block copolymer containing a PEG block and a NIPPAAm/ N-(2-hydroxypropyl)methacrylamide lactate block)page 7590, tables). The particle size after attachment of PEG 5,000 is only slightly greater than 100 nm (7590, col. 2), table); it is deemed inherent that without PEG the particle size is less than 100 nm. Neradovic also suggests that these micelles are useful as drug delivery systems (7589, col. 1, 7591, paragraphs bridging col. 1 and 2).

Neradovic does not specifically disclose the micelles in conjunction with a drug.

It would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to use the micelles of Neradovic to deliver drugs. The motivation is to follows the explicit suggestion of the prior art. Since Neradovic specifically suggests this manipulation, the artisan would enjoy a reasonable expectation of success.

Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Neradovic in view of Heller, US 5,939,453, of record.

The teachings of Neradovic are discussed above.

What is lacking is a teaching of an ABA block copolymer.

Heller teaches that AB and ABA block copolymers are equivalents in the art of forming polymer micelles.

It would be prime facie obvious to a person of ordinary skill in the art at the time of the invention to make the polymer of Neradovic as an ABA triblock copolymer rather than as an AB diblock. The motivation is that he two types of polymer architectures are recognized as equivalent in the art, and as such are considered to be obvious variants.

Therefore the artisan would enjoy a reasonable expectation of success at making the ABA copolymer, and would expect the ABA copolymer to have similar properties to the AB copolymer of the art.

Conclusion

Claims 1 – 12 are pending. Claims 1 – 4 are withdrawn. Claim 5 is objected to. Claims 5 – 12 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric E. Silverman, PhD whose telephone number is 571 272 5549. The examiner can normally be reached on Monday to Friday 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571 272 8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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